

## **Uncertainty in BRCA1 cancer susceptibility testing.**

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**This is the pre-peer reviewed version of the following article:**

Baty, B.J., W.N. Dudley, A. Musters, and A.Y. Kinney, Uncertainty in BRCA1 cancer susceptibility testing. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*, 2006. 142C(4): p. 241-250.

**which has been published in final form at:** <https://doi.org/10.1002/ajmg.c.30112>

### **Abstract:**

This study investigated uncertainty in individuals undergoing genetic counseling/testing for breast/ovarian cancer susceptibility. Sixty-three individuals from a single kindred with a known BRCA1 mutation rated uncertainty about 12 items on a five-point Likert scale before and 1 month after genetic counseling/testing. Factor analysis identified a five-item total uncertainty scale that was sensitive to changes before and after testing. The items in the scale were related to uncertainty about obtaining health care, positive changes after testing, and coping well with results. The majority of participants (76%) rated reducing uncertainty as an important reason for genetic testing. The importance of reducing uncertainty was stable across time and unrelated to anxiety or demographics. Yet, at baseline, total uncertainty was low and decreased after genetic counseling/testing ( $P = 0.004$ ). Analysis of individual items showed that after genetic counseling/testing, there was less uncertainty about the participant detecting cancer early ( $P = 0.005$ ) and coping well with their result ( $P < 0.001$ ). Our findings support the importance to clients of genetic counseling/testing as a means of reducing uncertainty. Testing may help clients to reduce the uncertainty about items they can control, and it may be important to differentiate the sources of uncertainty that are more or less controllable. Genetic counselors can help clients by providing anticipatory guidance about the role of uncertainty in genetic testing.

**Keywords:** genetic testing | cancer genetics | African Americans | cancer susceptibility | cancer testing | medical genetics | genetic counseling

### **Article:**

#### **INTRODUCTION**

Many practitioners believe that genetic testing has the potential to decrease uncertainty associated with genetic risk [Meissen et al., 1991; Decruyenaere et al., 1993; Baum et al., 1997]. This belief grows out of theories in the social sciences that were later applied to medicine [Lazarus and Folkman, 1984; Mishel, 1988, 1997, 1999; Hilton, 1994]. The medical and psychological literature suggest that uncertainty is a major cause of stress, that it decreases quality of life and psychosocial adjustment, and that it has an immobilizing effect on coping

processes [Lazarus and Folkman, 1984; Christman et al., 1988; Mishel, 1988, 1997, 1999; Hilton, 1994; Germino et al., 1998]. Uncertainty can limit the person's effective control and sense of control over the danger and thereby increase their feelings of helplessness and stress.

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In the 1980s and 1990s, Mishel 1981, 1990 wrote extensively about the uncertainty in Illness model, and developed an uncertainty scale. For a comprehensive review of studies of uncertainty in illness, uncertainty appraisal, and the relationship between uncertainty, coping, and adaptation, see Mast [1995]. Mast notes the lack of studies in multicultural populations or populations with few adaptive resources.

Many studies have shown that reducing uncertainty is a common reason cited by individuals utilizing genetic testing [Mastromauro et al., 1987; Meissen et al., 1991; Decruyenaere et al., 1993; Tibben et al., 1993; van der Steenstraten et al., 1994; Bernhardt et al., 1997; Tessaro et al., 1997]. However, several studies have suggested that genetic testing does not always result in a reduction in uncertainty [Wertz et al., 1984; Codori and Brandt, 1994; van Zuuren et al., 1997]. Other studies have suggested that in some instances, individuals with high uncertainty may avoid genetic testing [Croyle et al., 1995; Cypowyj et al., 2003]. In our clinical experience, clients typically describe the desired certainty in terms of settling whether or not they will develop the condition in question, but often ignore the other sources of uncertainty inherent in genetic testing. For example, uncertainty may also be associated with the maintenance of health, genetic transmission, lifestyle change (choosing surgery, more frequent screening and medical visits), reliability and mutation-specific effects of tests and test results, whether and when the feared condition develops after a positive test, and potential loss of insurance or employment as “payment” for medical knowledge. In spite of the widespread interest in genetic testing as a means of reducing uncertainty, few studies have examined clients' perceptions of uncertainty beyond the desire to reduce uncertainty and no studies have examined uncertainty before and after genetic counseling/testing.

Baum et al. [1997] propose a model that predicts long-term distress when risk analysis suggests a very high risk, when uncertainty is not reduced, when results of testing are at odds with

preventive actions already taken, and when people who receive a positive, risk-increasing result lack strong social support, coping skills, other psychosocial resources, or all of these. The model is based on Lazarus and Folkman's [1984] model of stress and coping.

The literature summarized above attests to the important role of uncertainty in genetic testing, yet more empiric evidence is needed to examine the complex role of uncertainty in the lives of individuals undergoing genetic counseling/testing. At the time this study was done there were no published measures of uncertainty that were specific to genetic counseling/testing. There is evidence that many consumers and providers of genetic counseling/testing value its role in reducing uncertainty, and there is also some evidence that genetic testing leaves tested individuals with considerable uncertainty.

The purpose of our study was to measure uncertainty about different aspects of genetic counseling/testing (access to medical care, insurance problems, inheritance, coping, desire for prophylactic surgeries, outcomes of testing) before and after testing from the perspective of individuals at high risk for carrying a BRCA1 mutation. Based on our clinical observations and knowledge of the literature available in 2001, we developed a series of 12 items to measure uncertainty associated with genetic counseling and cancer susceptibility testing.

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Our secondary aim was to determine the reliability and validity of the uncertainty scale we developed for potential future use as a measure of uncertainty related to genetic counseling/testing.

The uncertainty items related to the following observations:

1 Discussions with clients in the counseling session suggested that (a) a key concern for many clients was the likelihood of their children inheriting cancer susceptibility, (b) uncertainty about this risk appeared to be causing distress to the parent, and (c) parents expected the testing to help resolve the uncertainty.

2 Counselors often had lengthy discussions with clients about cancer prevention afforded by prophylactic mastectomy and/or oophorectomy, and clients frequently exhibited uncertainty about these surgical preventive options.

3 Many clients came to genetic counseling sessions with information or questions about the risk of insurance problems after genetic testing and we perceived uncertainty associated with this potential risk.

4 Clients often left a genetic counseling session with an expanded view of potential risks and benefits of testing and this sometimes appeared to engender uncertainty about experiencing positive and negative outcomes of testing.

5 Clients appeared to have variable degrees of trust in the medical system to provide optimal care and access to care. This has historically been of particular concern to African Americans, who typically have a higher degree of distrust of the medical system [Gamble, 1993; Thompson et al., 2003].

## STUDY HYPOTHESES

Our general hypothesis was that genetic counseling/testing does not reduce uncertainty, but rather reframes it. We developed the following specific hypotheses.

1 At baseline, the majority of study participants will cite decreasing uncertainty as an important reason for genetic testing.

2 Individuals with higher levels of uncertainty at baseline will be more likely to think decreasing uncertainty is important.

3 Total uncertainty will not decrease after genetic counseling/testing. Some individual uncertainty items will increase while others will decrease.

4 Variables associated with vulnerability (personal cancer history, family history, carrier status, medical insurance, perceived risk, cancer genetic knowledge, depression, anxiety, fatalism, religiosity, trust in doctor) will be associated with the total uncertainty score.

5 A decrease in anxiety will be associated with a decrease in uncertainty.

## METHODS

### Data Collection

Data were collected as part of a larger study of an African American kindred (Family Health Study) with more than 30 cases of breast/ovarian cancer and an identified BRCA1 mutation [Kinney et al., 2005, 2006]. The Family Health Study was a prospective observational cohort study that evaluated the extent to which culturally-sensitive genetic education, counseling and testing influence health behaviors and psychosocial outcomes among kindred members. The study was conducted after approval by Institutional Review Boards at the University of Utah (Utah) and Louisiana State University (LSU). Data was collected between 2001 and 2005. The main study offered genetic counseling and testing to individuals in the kindred and collected data using a computer assisted interview. These data were exported to SPSS [2004] and SAS [2002] for the analyses reported here.

## Sample

Our sample consisted of 63 individuals from a single African American (Creole) kindred. The choice of an African American kindred was a matter of convenience, as we were able to add our uncertainty items to a parent study of health behavior outcomes. One hundred five members of the kindred were initially enrolled and provided data before the first genetic counseling session (baseline). At follow-up, which was approximately 1 month (median 28.5 days) after testing (or genetic counseling, if testing was not done), 63 of the initial 105 (60%) provided follow-up data. The remaining 42 were either lost to follow-up ( $n = 21$ ) entirely or did not complete the 1-month interview but completed subsequent interviews ( $n = 21$ ). Those who did not complete the 1-month interview were younger than those who were retained (37.57 vs. 42.63,  $t(103) = 1.83$ ,  $P = 0.07$ ). Males were less likely to complete the 1-month interview than females (46% of males vs. 67% of females,  $\chi^2(1) = 4.46$ ,  $P = 0.04$ ). No differences between those who did not complete the 1-month interview and those who did were found in employment status, religious affiliation, marital status, income, carrier status (carrier vs. non-carrier), or importance of decreasing uncertainty as a reason for genetic testing. However, there were 18 individuals who did not have genetic testing, and none of them participated in the 1-month interview. The following results are reported for 63 participants who provided baseline and 1-month follow-up data. Some categories are missing data because participants did not answer all questions. Sample characteristics of the sample at baseline are provided in Table I.

Table I. Sample Characteristics

	Minimum	Maximum	Mean	Std. Dev
Age	18	82	42.6	15.0
Number of children	0	10	1.2	1.6
Number of daughters	0	4	0.6	0.9
Number of sons	0	6	0.6	1.0
		Frequency	Percent	
Gender				
Male		16	25.4	
Female		47	74.6	
Race				
Black or African American		63	100	
Ethnic background				
Creole		54	88.5	
Other		6	9.8	
None		1	1.6	
Hispanic				
Yes		0	0	
No		61	100	
Employment status				
Full time		37	58.7	
Part time		8	12.7	
Unemployed		2	3.2	
Retired		3	4.8	

	Minimum	Maximum	Mean	Std. Dev
In school		3	4.8	
Keep house		9	14.3	
Other		1	1.6	
Education				
Jr high school or less		1	1.6	
Some high school		8	9.5	
High school graduate		14	22.2	
Some college		27	42.9	
College graduate		11	17.5	
Post-graduate degree		2	3.2	
Religion				
Catholic		41	66.1	
Protestant		3	4.8	
Other		16	25.8	
Not a religious person		2	3.2	
Marital status				
Married		34	54.0	
Living as married		2	3.2	
Separated		2	3.2	
Divorced		4	6.3	
Widowed		6	9.5	
Never married		15	23.8	

	Minimum	Maximum	Mean	Std. Dev
Income				
Less than \$20,000		15	24.6	
\$20,000–\$40,000		18	29.5	
\$41,000–\$74,000		17	27.9	
More than \$75,000		11	18.0	
Covered by private health insurance				
Yes		40	63.5	
No		23	36.5	
Covered by public health insurance				
Yes		4	8.7	
No		42	91.3	
Carrier status by gender				
	Females		Males	
	N	%	N	%
Non-carriers	39	83.0	12	75.0
Carriers	8	17.0	4	25.0

## Measures

### Reasons for testing

In the parent study, individuals were asked to rate a list of possible reasons for genetic testing. The item related to uncertainty was to eliminate/reduce uncertainty. The responses for this item were 1 = “Not at all Important,” 2 = “Slightly Important,” 3 = “Somewhat Important,” 4 = “Important,” or 5 = “Very Important.” We used this item to determine whether study participants felt that decreasing uncertainty was an important reason for testing (hypothesis 1).



## Uncertainty related to genetic counseling/testing

In order to measure uncertainty related to multiple aspects of genetic counseling/testing and compare uncertainty before and after counseling/testing (hypothesis 3), we developed a 12-item measure related to uncertainty regarding genetic testing that were asked both at baseline and one-month follow-up (Table II). Participants were asked, “How certain or uncertain are you about the following statements?” For example, one uncertainty item was I can get the medical care I need to reduce my chances of getting cancer. Responses were 1 = “Very uncertain,” 2 = “Uncertain,” 3 = “Neither certain or uncertain,” 4 = “Certain,” or 5 = “Very certain.” These responses were later recoded from 5 “Very uncertain” to 1 “Very certain” so that our analysis reflects uncertainty rather than certainty. Mean scores for all participants answering the item were compared for individual items at baseline and 1-month follow-up.

**Table II. Uncertainty Items**

How certain or uncertain are you about the following statements?

1. My daughters/future daughters will inherit the BRCA1 gene change or alteration in my family
  2. My sons/future sons will inherit the BRCA1 gene change or alteration in my family
  3. I am unlikely to have problems with insurance because of BRCA1 testing
  4. I know whether I want to have preventive surgery to avoid the risk of cancer
  5. Learning my chances of getting cancer will [has] negatively affect[ed] my life
  6. \*I can get the medical care I need to reduce my chances of getting cancer
  7. \*I can get the cancer screening I need (like mammograms, breast exam, or blood tests) to increase my chances of early diagnosis if I do get cancer
  8. \*\*I will cope [am coping] well with my genetic test result
  9. \*\*I will have [have had] positive changes in my life after learning the results of my genetic test
  10. \*\*I will be able to detect signs of cancer early
  11. \*\*I will follow through with recommended cancer detection check ups
  12. \*\*My physician or health care provider will be able to detect signs of cancer early
1. Very certain
  2. Certain
  3. Neither certain or uncertain

4. Uncertain

5. Very uncertain

Square brackets reflect the way the item was phrased at time 2. Using factor analysis, \* and \*\* indicate clusters

Instrument refinement for the measurement of uncertainty was conducted on all baseline data to capitalize on the larger sample ( $n = 105$ ). For pooled comparisons regarding associations between total uncertainty and the desire to decrease uncertainty (hypothesis 2), vulnerability variables (hypothesis 4), anxiety (hypothesis 5), and demographic variables, our initial pool of 12 items was first reduced to a set of 7 as follows. Three items were missing data for 20% or more of the sample. These items are numbered 1, 2, and 4 in Table II. Although reasons why participants declined to answer these items are unknown, we assume that those respondents without sons or daughters or planning not to have children did not provide data to items 1 or 2. Missing data for item 4 (regarding preventative surgery) was strongly gender related with 86% of males missing data and only 3% of females missing data. This suggests that males did not think preventative surgery was pertinent to them. Thus items 1 and 2 were eliminated because they were not applicable to many participants and were thus missing. Items 3, 4, and 5 were eliminated because they show corrected item to total correlations below 0.2. This resulted in a measure of uncertainty of seven items which are indicated by asterisks in Table II. Exploratory factor analysis (using maximum likelihood estimation and varimax rotation) was used to examine the factor structure of these seven items. There was some evidence of a two factor structure in that two eigenvalues were greater than one and there was a significant improvement in goodness of fit with the two factor solution ( $\chi^2(14) = 39.6$  for the one factor and  $\chi^2(8) = 17.0$  for the two factor solution). In this two factor solution, we termed the first factor with two items (indicated by single asterisks) as an Access Uncertainty factor. These two items were related to uncertainty about access to appropriate medical care. We characterized the second factor with five items (shown as two asterisks in Table I) as a Control Uncertainty factor. These items related to uncertainty about the control the client has to cope, follow through with recommendations, and detect cancer early. Further evaluation of these two scales indicated that both scales were at the low end of acceptable internal consistency reliability for a newly developed scale (Cronbach's  $\alpha = 0.62$  and  $0.65$  for Control Uncertainty and Access Uncertainty, respectively) [Nunnally and Bernstein, 1994]. The Control Uncertainty factor showed better sensitivity to change than the two item Access Uncertainty scale or the total of the seven items taken together, and thus we report results from that five-item scale as the total uncertainty score.

Psychological well-being

Anxiety was measured using the 20-item state anxiety scale of the State-Trait Anxiety Inventory STAI—Form Y [Spielberger et al., 1971]. The STAI is the most widely used measure of anxiety. The presence of depressive symptoms was measured using the CES-D Scale (Center for Epidemiological Studies Depression Scale) [Radloff, 1977]. This scale was developed for use in the general population to measure symptoms of depression with a focus on affective components, including feeling depressed, hopeless, fearful, or sad. This scale has been used extensively in social science research and internal consistency was high ( $\alpha = 0.87$ ) in a previous pilot study of this kindred [Kinney et al., 2005]. These scales were used together as a measure of psychological well-being. We examined whether there was an association between the change in total uncertainty and the change in distress before and after counseling/testing (hypothesis 5).

### Fatalism

Cancer fatalism was measured with the 15-item Powe [1995] Fatalism Inventory, composed of four subscales that measure fear about cancer, cancer pessimism, predetermination, and inevitability of death using a yes/no format ( $\alpha = 0.73$ ). This instrument has established reliability and validity in African Americans (Chronbach's  $\alpha = 0.84$ – $0.87$ ).

### Hereditary cancer knowledge

A 10-item knowledge questionnaire developed by the Cancer Genetics Consortium and adapted for this study was used to assess knowledge about hereditary breast and ovarian cancer [Lerman et al., 1996].

### Perceived cancer risk

Perceived risk was measured using two questions for breast cancer, In your opinion, how likely is it that you will develop breast cancer in your lifetime? (Very unlikely, Unlikely, Moderate Chance, Likely, Very likely, I have already had breast cancer), and What do you think the chances are the you will get breast cancer sometime during your lifetime? (Percent, Has had both breasts removed), and the equivalent questions for ovarian cancer. These questions have been used in several other studies to measure risk perception [Codori et al., 1999; Durfy et al., 1999], including high-risk African Americans [Hughes et al., 1996].

### Trust of health care providers

Trust in medical care providers was measured by a six item Likert type scale adopted from Safran et al. [1998]. An example item was worded, “My doctor cares as much as I do about my health.” Response ranged from 1, “Strongly disagree” to 5, “Strongly Agree.” The scale showed acceptable internal consistency (Cronbach's alpha = 0.83). All items were recoded such that higher values indicated higher trust. The total score was a simple total of all items and ranged from 1 to 20 (mean = 12.79, SD = 3.86).

## Religiosity

Religiosity was measured using a four-item scale. A sample item was worded, “How strong would you say your religious or spiritual faith is?” Responses to these items ranged from 1, “Not at all strong” to 4, “Very strong.” The scale showed good reliability (Cronbach's alpha = 0.81). All items were recoded such that higher values indicated higher religiosity. The scale was created as a sum of all items. The range for the sample was 1–12 (mean = 9.48, SD = 2.62).

## Statistical Analysis

We used McNemar's exact test [Pett, 1997] to compare the binary variables' importance of reducing uncertainty at baseline with responses at 1-month (related to hypothesis 1). The association between the perceived importance of genetic testing in reducing uncertainty and total uncertainty scores (hypothesis 2) was evaluated using Spearman Correlation. We examined changes from baseline to follow-up in the responses across all uncertainty items (hypothesis 3) using t-tests. Considering baseline total uncertainty score as a continuous variable, Pearson correlations were performed with other continuous (or close) variables (age, number of children, education, income, knowledge of cancer genetics, religiosity, perceived risk, depression, trust in doctor, and cancer fatalism) (hypothesis 4). ANOVAs were performed with categorical variables (marital status, personal cancer history, presence or absence of first degree relatives, BRCA1 carrier status, employment, and presence or absence of medical insurance) (hypothesis 4 and demographic variables). The association between the STAI or the CES-D Scale and total uncertainty scores (hypothesis 5) were evaluated using Pearson's correlation. For all analyses, results were considered significant if the P-value was  $\leq 0.05$ .

## RESULTS

### Sample Characteristics

The study population of this single kindred was 75% female and 100% African American. The mean age was 42.6 (SD 15.0) and mean number of children was 1.2. Most were employed (71.4%; 9.6% were retired or in school) and had at least a high school education (85.8%). About half were married, 96.7% listed a religion and incomes were varied. Sixty-four percent had private health insurance and 9% had public health insurance. Fifty one (81%) were non-carriers; 12 (19%) were carriers. The data were gathered from 29 sibling groups. Fifty-two participants had at least one other sibling in the study. The number of siblings ranged from zero to five. The majority of groups had zero or one sibling (52%), and the mean sibling group size was 1.17. The sibling indicator was used in the analyses reported below to control for within family (at the sibling level) correlations.

### Importance of Reducing Uncertainty

At baseline, the vast majority (76%) of individuals thought that reducing uncertainty was either an important or very important reason for genetic testing. This rating of the importance of reducing uncertainty at baseline did not differ by age, gender, marital status, income, education, or work status.

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When comparing the importance of reducing uncertainty at baseline with responses at 1-month following receipt of test results we found no differences in the rating of importance over time ( $P = 0.95$ ). In addition, we found no relationship between state anxiety and importance of genetic testing in reducing uncertainty either at either baseline or follow-up. Thus, the importance of reducing uncertainty was rated as very high by participants, was stable across time, and was unrelated to individual-level demographics or anxiety.

### Comparison of Uncertainty Items Before Genetic Counseling/Testing (Baseline)

For those who answered all of the uncertainty items at both baseline and follow-up ( $n = 63$ ), the internal consistency reliability was 0.70 at baseline and 0.81 at follow-up. The total uncertainty score was computed as the mean score of each of the answered items such that high scores indicate high uncertainty. The highest score at baseline was 4.4 and the lowest score was 1.0,

with a mean of 2.34 (sd = 0.66) across the five items for all participants. The highest score at follow-up was 4.8, and the lowest score was 1.0, with a mean of 2.03 (sd = 0.73). Thus on average, participants reported a low level of uncertainty on the five items at follow-up.

When the individual items were ranked by mean uncertainty at baseline, the means ranged from 2.85 to 1.86 (Fig. 1). The highest uncertainty was for the ability of the participant to detect cancer early. The lowest uncertainty was for the ability to follow through with the recommended cancer detection check ups.

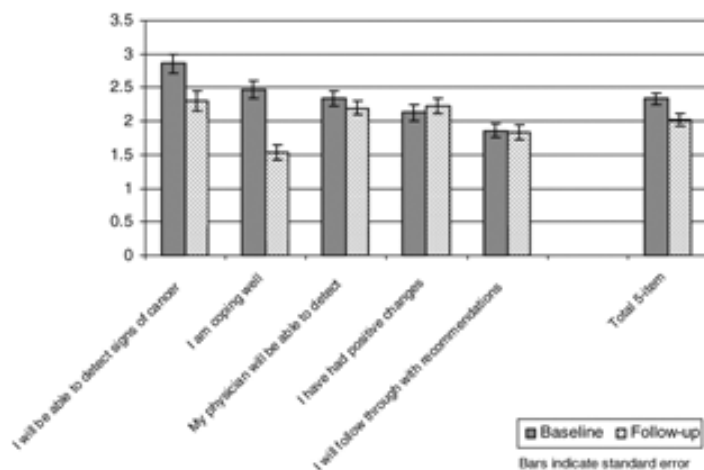


Figure 1. Percent of respondents who are uncertain for each item at time 1 and time 2.

#### Changes in Uncertainty Before and After Genetic Counseling/Testing

Mean uncertainty at follow-up for the five individual items ranged from 2.31 to 1.83. Given the importance of reducing uncertainty as indicated by the participants, we examined changes in uncertainty for all five individual items. Significant decreases in uncertainty over time were observed for item 8 “I am coping well with my genetic test result” ( $P < 0.001$ ) and item 10 “I will be able to detect signs of cancer early” ( $P = 0.005$ ). There were no significant differences in the remaining individual items. Total uncertainty decreased significantly from a mean of 2.34 to 2.03 ( $P = 0.004$ ) (Table III). There were no gender differences in total uncertainty at baseline or one-month follow-up and no gender differences in the change in total uncertainty between baseline and follow-up.

**Table III is omitted from this formatted document.**

#### Correlates of Uncertainty

We examined demographic variables and variables related to possible increased vulnerability (being a carrier, being older, having less adequate medical insurance, having more children, having higher perceived cancer risk, and having higher depression scores, more positive family

cancer history, a personal history of cancer, more cancer genetic knowledge, and more fatalism) and decreased vulnerability (being married, having more education, having higher income, being employed, a higher degree of religiosity, more trust in doctor). There was more baseline uncertainty in individuals with more children ( $P = 0.02$ ). None of the other analyses attained significance.

### Importance of Reducing Uncertainty

There was no correlation between perceived importance of genetic testing in reducing uncertainty and the level of uncertainty as measured by the five-item total uncertainty scale.

### Change in Uncertainty Related to Distress and Carrier Status

Correlation of change scores in uncertainty and anxiety showed no relationship ( $r = 0.18$ ), nor did uncertainty and depression ( $r = 0.185$ ). The association between change in uncertainty and carrier status was examined using a repeated measures ANOVA with total uncertainty at baseline and time two and carrier status as a single binary independent variable. The results indicated no relationship between change over time and carrier status. The time by carrier status interaction was not significant;  $F(1, 61) = 0.08$ ,  $P = 0.78$ .

## DISCUSSION

In 2001 we scoured the literature for a validated scale to measure uncertainty associated with genetic counseling/testing. Although the scales developed by Mishel had been widely used, the items on the scale did not measure uncertainty related to genetic counseling/testing. In 2002, Cella et al. [2002] developed a nine-item uncertainty subscale of the multidimensional impact of cancer risk assessment (MICRA) tool to measure the specific impact of result disclosure after genetic testing. Individuals who tested BRCA1/2 positive had higher scores than individuals who tested negative. They suggest that the subscale may help differentiate a subset of participants who need intervention and/or are at risk for future distress. Interestingly, the MICRA uncertainty subscale did not differentiate individuals with true negative results from individuals with uninformative negative results. Since uninformative negative results are much more uncertain than true negative results, one would expect the scale to differentiate these two categories of study participants. In the absence of an alternative, we developed a measure of uncertainty based on our clinical experience with cancer genetics clients from a previous study [Botkin et al., 1996]. This offers a useful opportunity for comparison to the results reported by Cella and colleagues who used a different but related measure.

As expected from the experience of others [Mastromauro et al., 1987; Meissen et al., 1991; Decruyenaere et al., 1993; Tibben et al., 1993; van der Steenstraten et al., 1994; Bernhardt et al., 1997; Tessaro et al., 1997], our data supported our first hypothesis. The vast majority of our study participants (76%) listed decreasing uncertainty as an important reason for testing. Hughes et al. [1997] also found that about 80% of African American women in their study listed reducing uncertainty as very important compared to about 65% of Caucasian women.

Our second hypothesis was that individuals with higher uncertainty at baseline would be more likely to think decreasing uncertainty is important. Instead, we found no correlation. It is possible that individuals with more uncertainty did not believe that genetic testing would reduce their uncertainty (similar to the research participants in Croyle et al., 1995) or were more comfortable with their level of uncertainty.

Our second hypothesis was that individuals with higher uncertainty at baseline would be more likely to think decreasing uncertainty is important. Instead, we found no correlation. It is possible that individuals with more uncertainty did not believe that genetic testing would reduce their uncertainty or were more comfortable with their level of uncertainty.

Another possibility is that the uncertainty scale and the importance measure were measuring uncertainty about different aspects of genetic testing. When asked to rate the importance of decreasing uncertainty, study participants might think only of the uncertainty of whether or not they inherited the cancer susceptibility in their family, while our uncertainty items measured uncertainty about obtaining healthcare, the expectation of positive changes, and coping well with results.

Our third hypothesis was that changes in uncertainty from baseline to one month would increase in some areas and decrease in other areas. Our clinical experience was that individuals first focus on the uncertainty of whether or not they have a disease causing or susceptibility gene mutation. Once they learn that they are positive, their uncertainty often shifts to other areas, such as whether they can obtain medical care that will help them avoid or survive the condition, and how they will cope with the result. When we assessed our total uncertainty scale, we found that two of the individual items decreased, total uncertainty decreased, and no individual uncertainty items increased. This outcome of decreased uncertainty could be due to the high proportion of individuals in our study who did not carry the gene mutation, although our finding of no association between carrier status and total uncertainty argues against this explanation.



We chose to use the Control Uncertainty factor as our measure of total uncertainty, since it performed cohesively and was most responsive to change before and after testing. The total uncertainty score was low, averaging 2.34 at baseline, and decreased to 2.03 at follow-up. It is possible that genetic counseling helped decrease uncertainty further by increasing trust in participants' ability to obtain appropriate medical resources and participants' ability to cope with the risk in their family and/or outcome of testing. This Control Uncertainty factor may be related to the idea of perceived personal control (PPC) introduced to the genetic counseling literature by Berkenstadt et al. [1999]. They described the concept of PPC and adapted it to genetic counseling. They found higher post-counseling PPC among counselees who had been given a definite diagnosis, a specific recurrence risk, and been offered prenatal diagnosis. These factors are also associated with lower uncertainty. Although we did not measure PPC, our study participants' decrease in Control Uncertainty after genetic counseling/testing may be due to a similar phenomenon.

Baseline uncertainty was higher in individuals with more children, while all other variables examined showed no correlation with baseline uncertainty (hypothesis 4). It is not obvious why having more children is associated with higher total uncertainty. Individuals with more children may have more uncertainty about positive outcomes because of stronger concerns about their children's welfare than their own welfare. In our experience counseling families at high risk for family specific BRCA1 mutations, concerns about children come up frequently in counseling and parents often verbalize more concern about their children's risks than their own risks.

Both carriers and non-carriers reported significantly fewer symptoms of anxiety at 1 month compared to baseline [Kinney et al., 2005]. Our last hypothesis was that a decrease in anxiety and depressive symptoms would be positively associated with a decrease in global uncertainty, since uncertainty has been shown to cause more distress than either positive or negative genetic test results. However, no correlation was found. Baum et al.'s [1997] model predicts that a reduction in uncertainty will help reduce distress. They also state that getting a clear outcome reduces uncertainty regardless of whether one's risk is increased or decreased, but note that research has not directly evaluated this hypothesis. Our findings of a general decrease in uncertainty and no correlation between uncertainty and carrier status support this hypothesis.

Our findings have several implications for clinical practice. They continue to support the importance to clients of genetic counseling/testing as a means of reducing uncertainty. This replicates the findings of Hughes et al. [1997] that this expectation may be even higher in

African American clients. Our findings that uncertainty about medical care and coping with test results was relatively low and decreased after counseling/testing bore out the expectations of these clients. Genetic counselors can provide anticipatory guidance about uncertainty associated with genetic testing and assess whether their clients expect genetic testing to decrease uncertainty, what aspects of uncertainty they think will be reduced, and how important it is to the client to reduce uncertainty.

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Items that clustered together and had the highest change scores shared the characteristic of being associated with client control. Testing may help clients to reduce the uncertainty about items they can control, and it may be important to differentiate the sources of uncertainty that are more or less controllable.

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Areas for future research include examining uncertainty in other genetic conditions, in a larger sample of individuals with positive genetic test results, and in relation to PPC and client satisfaction, as well as testing counseling interventions to reduce client uncertainty. It would also be useful to develop scales that reliably measure other aspects of uncertainty related to genetic counseling and testing, and to differentiate uncertainty related to genetic counseling versus genetic testing.

### Study Limitations

The study consists of a relatively small sample size, with all participants being members of a single kindred of African American (Creole) ethnicity. Although we were focused on the general topic of uncertainty rather than uncertainty specific to this ethnic group, we recognize that these findings may not be representative of all individuals, or all African Americans. In addition, many members of this kindred participated in a previous linkage study, although they were not given genetic counseling or test results at the time of that study. Their previous knowledge and

experience with genetic testing may be higher than individuals with no previous exposure to genetic research. Although this limits generalizability, it also increases our understanding of cancer genetic testing offered to both female and male members of a minority ethnic group. All participants were counseled/tested in a research setting, which may have significant differences from a clinical setting. We had a low number of positive BRCA1 test results in our sample, which limits the statistical power of the analysis of the effects of mutation status post-testing.

Another limitation of the study is that we did not separate the effects of genetic counseling and genetic testing. Although the literature focuses on uncertainty associated with genetic testing, it is likely that genetic counseling affects clients' uncertainty about many aspects of genetic testing. For example, a client might learn about additional resources for coping with a positive test result (reducing uncertainty), but might also learn that testing will not tell her whether or not she will develop cancer (increasing uncertainty).

## SUMMARY

Both before and after genetic counseling and/or testing, the vast majority of individuals in the study felt that reducing uncertainty is an important reason for genetic testing. The importance of reducing uncertainty was stable across time and unrelated to anxiety or demographics. Factor analysis identified a five-item total uncertainty scale that was sensitive to changes before and after testing. The items in the scale were related to uncertainty about obtaining health care, positive changes after testing, and coping well with results. Overall, we found that study participants revealed a low level of uncertainty regarding genetic testing and total uncertainty decreased after genetic counseling and/or testing. After genetic counseling/testing, there was less uncertainty about the ability of participants to detect cancer early and to cope well with a positive result, compared to before genetic counseling/testing. Further research into the complexity of clients' uncertainty about genetic testing will help understand the views of individuals undergoing genetic counseling/testing and inform interventions to help them manage uncertainty.

## Acknowledgements

We are grateful to Dr. Diptasri Mandal, Dr. Jeffrey Botkin, Dr. Lee Ellington, Dr. Susan Neuhausen, and Dr. Ken Smith as well as Sara Ellis, Kate Seggar, and Jean Wylie for their assistance with the design and implementation of the project, the genetic counselors (Regan

Challinor and Kelly Jackson), the medical geneticist (Mary K. Pelias), the interviewers (Andrea Wiley, Berneice Parker, Kendra Rockwell, Josalin Hunter, Ashley Holmes, Carolyn Ross, Jucynthia Taylor Ford), and all of the family members of K2099 who participated in this study.

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